REMARKS/ARGUMENTS

Claims 71-74, 76-77, and 79-82 are pending and under examination.

Interview

Applicants thank Examiner Susan Ungar for the courtesy of a telephonic interview with the undersigned on January 28, 2008. All of the claims were discussed. As explained in the Examiner's interview summary (a copy of which is enclosed), Examiner Ungar:

- Agreed the term "adaptive immune response" was not indefinite.

- Agreed that the new matter rejection of claims 79-82 should be withdrawn.

- Agreed that claims 71-73, 79, and 81-82 would be allowable upon submission of a terminal disclaimer over US Pat. No. 6,261,836 and pending an interference search.

Claim amendments

For additional clarity claims 71-74, 75 and 77 have been amended to make explicit that the hTRT-encoding sequence is operably linked to a promoter. This was inherent in the claims as previously pending. Upon administration of the claimed composition to a human or non-human animal the nucleic acid sequence is expressed and translated by host cells, and an adaptive immune response is mounted against the hTRT antigen. Support is found in the specification (*e.g.*, paragraphs [0299] and [0179] *et seq.* of the published specification, US Pat. App. Pub. 2003-0096344). Claims 79-82 have been similarly amended to make explicit that the hTRT-encoding sequence is expressed, as was inherent in the claims as previously pending.

Remaining Issues

Agreement was not reached during the interview with regard to claims 74, 76, 77, and 80. These claims were rejected under 35 USC 112, 1st paragraph as allegedly not described in the specification.[1] The written description requirement of Section 112, first paragraph, requires that

[1] The Office Action states the claims are rejected "for reasons previously set forth in the paper mailed January 18, 2007, Section 4, pgs 2-6." Section 4 of the paper mailed January 18, 2007 states the claims are rejected for "the reasons previously set forth in the paper mailed April 21, 2005, Section 9, pages 9-12." As Applicants have previously respectfully noted, this is confusing because Section 9 of the 2005

the specification describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. Examiner Ungar in the Office Action acknowledged the Inventors' possession of polypeptide fragments of full-length hTRT consisting of at least 10 amino acids of hTRT.[2] She also acknowledged that a composition comprising a nucleic acid encoding the full-length hTRT would elicit an adaptive immune response when administered to a subject and that fragments of SEQ ID NO:2 would elicit an adaptive immune response against themselves.

Examiner Ungar argued, however, that although one of skill reading the specification would immediately envision fragments of SEQ ID NO:2, "one would not immediately envision immunogenic fragments that will elicit an adaptive immune response against SEQ ID NO:2."[3] Examiner Ungar also stated the specification provided "no guidance drawn to the fragments that will function as claimed" (*i.e.*, which fragments will elicit an adaptive immune response).[4] Examiner Ungar also argued that it was unpredictable that antibodies elicited by "linear" hTRT peptides will bind to the full length antigen.[5] Finally, Examiner Ungar asserted that nucleic acids encoding a polypeptide "comprising" at least 10 contiguous amino acids of SEQ. ID NO:2 was "clearly undefined" because, she asserted, "it is not possible to determine the structures of

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Office Action addressed claims different from those now under examination. Indeed, each of the Office Actions has presented different and diverse arguments.

[2] For consistency with the language used by the Examiner, this response frames parts of the discussion in terms of hTRT polypeptide fragments. It will be understood that the claims are directed to compositions containing a *nucleic acid encoding* a polypeptide that comprises an hTRT fragment (at least 10 contiguous amino acids of SEQ. ID NO:2) wherein the composition elicits an adaptive immune response against hTRT when administered to a subject.

[3] Pages 2-3 of the Office Action.

[4] Page 3 of the Office Action. The current Examiner is reminded that at the time Examiner Ungar articulated this position she had also argued that the meaning of "adaptive immune response" was unclear. She subsequently recognized that "adaptive immune response" was a well known term in the art of immunology and withdrew from this position.

[5] Page 3 of the Office Action.

fragments "'comprising" or to determine the effect of additional amino acids on the immunogenicity of the claimed fragments "comprising."[6]

Applicants respectfully disagree with the position of Examiner Ungar. Examiner Ungar acknowledged that full-length hTRT (1132 amino acids in length) will elicit an adaptive immune response. Applicants believe it would not be disputed by the Office that a fragment consisting of 1131 amino acids would also be immunogenic. The first concern of the Office appears to be that some small fragments might not elicit an adaptive immune response against hTRT or might not elicit an adaptive immune response that would include antibodies that recognize hTRT in the native conformation.

Initially, Applicants point out that the claims do not require that antibodies elicited by the claimed compositions bind hTRT in the native conformation. Antibodies that bind denatured hTRT are also useful.

Further, as evidence that a short peptide might not elicit an immune response that recognizes native human TRT, Examiner Ungar cited Holmes et al., 2001, *Exp. Opin. Invest. Drugs* 10(3):511-519, as teaching that "none of the antibodies [generated by synthetic peptides] exhibited binding to the full length antigen."[7] Applicants submit that although the antibodies described in Holmes did not bind to full length protein, this does not indicate that antibodies generated by the peptides of the claimed invention would not bind to full length protein. The synthetic peptides used in Holmes, aa63-68, aa132-137 or aa482-487 (p. 513, col. 1) consist of only 5 amino acids rather than polypeptides that are at least 10 consecutive amino acids in length as claimed in the present invention. In fact, the Holmes et al. reference concluded that "The observation ... perhaps can be overcome by the use of slightly longer eight amino acid peptides as was utilized by Murphy et al." (p. 513, col. 1). Holmes also teaches that the antibody utilized by Murphy was capable of immunoprecipitating native full length protein (p. 512, col. 2). Thus, the Holmes et al. reference does not support the Examiner's assertions.

[6] Page 3 of the Office Action.

[7] Page 4 of the Office Action.

Applicants submit that, provided with the disclosure of the hTRT protein sequence --a discovery of enormous scientific and medical significance-- and the teachings of the lengthy specification, one of skill in the art would have recognized the inventors' had "possession" of hTRT fragments that will elicit an adaptive immune response in humans and other animals. Moreover, methods of determining immunogenic portions of protein antigens are described in the specification and were well known in the art. This knowledge includes how to determine the ability of an hTRT fragment to generate both T-cell and B-cell immune response. For example, immunogenicity of an hTRT fragment can be determined at a practical level by injecting the fragment and an adjuvant into an animal and then assaying for the appearance of antibodies directed against the injected peptide (see the specification at, e.g., paragraphs [0204]).

Having been provided by the inventors with the (previously unknown) sequence of hTRT, one of skill at the priority date of the invention would have been able to use art-known methods to predict fragments that were likely to be most immunogenic. For example, a copy of pages 25-52 of a text book entitled "Vaccine Design" (1993) by F. Brown et al. is provided in the supplemental information disclosure statement (IDS) concurrently submitted. Chapter 4 of this reference explains how epitopes can be predicted from amino acid sequence information. The common knowledge of one of ordinary skill in the art would have included the prediction of B-cell epitopes and/or T-cell epitopes in a full length protein. Specifically, one skilled in the art could have predicted the most likely linear (B-cell) epitopes using the sorts of procedures described on pages 34-38 of "Vaccine Design." T-cell epitopes could have been predicted by the procedures described on pages 39-43 of this reference.

As a practical matter, the average skilled person would have been able to use algorithms that not only identified MHC binding motifs, but were also able to rank them according to relative binding strength. For example, Parker et al.[8] (*J. Immunol.* 152:163-175 (1994)) discusses a scheme for ranking potential HLA-A2 binding peptides. Numerous publications in the art disclosing algorithms for peptides with MHC II binding motifs (see, *e.g.*, Davenport et al., 1995, *Immunogenetics* 42:392-397; Meister et al., 1995, *Vaccine* 13: 581-591; and pages 76-78 of

[8] Parker et al. and the other references cited in this paragraph are provided in the concurrently filed supplemental information disclosure statement (IDS).

Hammer et al., 1997, *Advances in Immunology* 66:67-100). Furthermore, it was standard practice to identify peptides comprising MHC binding motifs by generating overlapping peptides spanning the sequence of a protein antigen and then test these peptides for the ability to stimulate a T-cell response (see Meister, page 581, paragraph 2). This peptide search technique predicted all the known T-cell epitopes in five model proteins tested (see Table 3 of Meister). Based on at least these reasons, it would have been clear to the skilled artisan that the inventors, having cloned and characterized the human TRT gene, could select immunogenic fragments of SEQ ID NO:2.

Thus, one of skill in the art reading the specification would have recognized that Applicants invented what is now claimed.

With respect to the "comprising" language of claims 76 and 80, Examiner Ungar asserted that "the fragments 'comprising' at least 10 amino acids of SEQ ID NO:2 are clearly undefined because it is not possible to determine the structures of those fragments 'comprising' or to determine the effect of additional amino acids on the immunogenicity of the claimed fragments 'comprising'."

With regard to the term "comprising," Applicants respectfully submit that the written description requirement does not preclude the use of open claim language. In the instant claims, the structure of the fragments are specifically defined by sequence, *i.e.*, they comprise from 10 to 1131 contiguous residues of SEQ ID NO: 2.[9] By way of analogy, if an applicant claimed an invention that is "a formulation *comprising* 10-15% sucrose and 60-70% sodium chloride" this clearly would not be a violation of the requirements of Section 112, first paragraph. In the instant case, the claims are drawn to a composition comprising a nucleic acid encoding a polypeptide that comprises at least 10 contiguous amino acids of SEQ. ID NO:2, where the

[9] More precisely, the claimed compositions contain nucleic acids that encode hTRT sequences and may encode additional amino acids. Again, Applicants note that for consistency with the language used in the Office Action, this discussion is framed in terms of polypeptide fragments of hTRT. It will be understood that that claims are in fact directed to *compositions* containing a *nucleic acid* encoding a polypeptide that comprises at least 10 contiguous amino acids of SEQ. ID NO:2, wherein the composition elicits an adaptive immune response against hTRT when administered to a subject.

composition elicits an adaptive immune response against hTRT (SEQ. ID NO:2) when administered to a subject. Thus, the claimed subject matter is described by structure ("at least 10 contiguous amino acids of SEQ. ID NO:2") and properties ("the composition elicits an adaptive immune response against hTRT") and a clear correlation between the structure of the fragments and their function is provided. This meets the requirements of Section 112, first paragraph.

Examiner Ungar also argued that it was not possible to determine the effect of additional amino acids on the immunogenicity of the claimed fragments.[10] Examiner Ungar did not explain what "effect of additional amino acids" was being referred to. Applicants submit it is routine to use, for example, fusion proteins to elicit an immune response to a specified polypeptide sequence of the fusion protein. Even if one could imagine it is possible that some additional residues could negate immunogenicity (and thus not be encompassed by the language of the claims) it is not apparent how this would relate to the written description requirement.

In summary, Section 112 requires that the applicant has conveyed to those of skill in the art that he or she was in possession of the claimed invention at the time of filing. The identification by the inventors of human telomerase reverse transcriptase (hTRT) was a scientific breakthrough and one of the seminal achievements of the late 1990s. In a lengthy and detailed specification Applicants disclosed the use of hTRT polypeptides and polynucleotides to, *inter alia*, elicit an immune response. Applicants submit one of skill reading the specification would clearly recognize the inventors' "possession" of the claimed subject matter.

Applicants respectfully request this rejection be withdrawn.

Double patenting

The claims were also rejected under the doctrine of Obviousness Type Double Patenting over US Pat. No. 6,261836. Applicants will provide a terminal disclaimer or otherwise respond to this rejection upon indication that the claims are otherwise allowable.

[10] Page 3 of the Office Action.

CONCLUSION

For the reasons provided above, Applicants respectfully request that the claims now pending be examined and a Notice of Allowance issued.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-462-5330.

Respectfully submitted,

Randolph Ted Apple
Reg. No. 36,429

Encls.

Examiner Interview Summary

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D:Ted Apple COMPANY:

COPY

US App. No. 10/044,692
Attachment to Amendment
Filed March 20, 2008

Patent Technology Centers

Facsimile Transmission

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37 C.F.R. 1.6 sets forth the types of correspondence that can be communicated to the Patent and Trademark Office via facsimile transmissions. Applicants are advised to use the certificate of facsimile transmission procedures when submitting a reply to a non-final or final Office action by facsimile (37 CFR 1.8(a)).

Fax Notes:

Attached please find the summary of the interview that we had today on US Application 10/044692.

Thank you for your interest. Any questions just give me a buzz at 571-272-0837. I will be available through Wednesday, January 30, COB.

Susan Ungar
Primary Patent Examiner
1642

Date and time of transmission: Monday, January 28, 2008 12:38:26 PM
Number of pages including this cover sheet: 04

Interview Summary	Application No.	Applicant(s)	
	10/044,692	CECH ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

All participants (applicant, applicant's representative, PTO personnel):

(1) *Susan Ungar*. (3)_____.

(2) *Ted Apple*. (4)_____.

Date of Interview: *28 January 2008*.

Type: a)☒ Telephonic b)☐ Video Conference
c)☐ Personal [copy given to: 1)☐ applicant 2)☒ applicant's representative]

Exhibit shown or demonstration conducted: d)☐ Yes e)☐ No.
If Yes, brief description: _____.

Claim(s) discussed: *All pending*.

Identification of prior art discussed: _____.

Agreement with respect to the claims f)☐ was reached. g)☐ was not reached. h)☐ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: *See Continuation Sheet*.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN A NON-EXTENDABLE PERIOD OF THE LONGER OF ONE MONTH OR THIRTY DAYS FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

_____
Examiner's signature, if required

O:Ted Apple COMPANY:

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews
Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

.37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

Continuation Sheet (PTOL-413) **Application No. 10/044,692**

Continuation of Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: Discussed current rejections. Upon review of the art and reconsideration, it has been found that language drawn to adaptive immune response is in fact not indefinite because the art clearly demonstrates, in dozens of articles that this is a conventional term of the art wherein the art recognizes that "Adaptive immunity refers to antigen-specific immune response. The adaptive immune response is more complex than the innate. The antigen first must be processed and recognized. Once an antigen has been recognized, the adaptive immune system creates an army of immune cells specifically designed to attack that antigen. Adaptive immunity also includes a "memory" that makes future responses against a specific antigen more efficient" (see http://www.biology.arizona.edu/immunology/tutorials/immunology/page3.html). Further, it appears that, upon submission of a terminal disclaimer over US Patent No.6,261,836, claims 71 and 72 would appear to be allowable pending final interference search. Further given the QUAS consensus decision of late January, 2008, it would appear that claim 73 indeed is enabled and has written description since claim 73 is in line with Example 14 of the current guidelines and in accordance with the Kubin decision. Finally, in terms of the composition comprising the plasmid vector recited in claims 79-82, upon review and reconsideration it would appear appropriate to withdraw this new matter rejection given that the claimed limitations in fact flow from the specification as orginally filed. Further in line with the parallel claims 71-73, it would appear that claims 79, 81-82 would be allowable pending interference search....